REMARKS/ARGUMENTS

Claim 72 has been amended to remove reference to "a fraction of their respective ED_{50} values." Accordingly, this amendment does not introduce new matter.

Claims 67-88 are pending in the application. Reconsideration of the claims is respectfully requested in view of the above-referenced claim amendment and the following remarks. The Examiner's comments in the Office Action are addressed below in the order set forth therein.

The Rejection of the Claims Under 35 U.S.C. §112, First Paragraph, Should Be Withdrawn

Claim 72 is rejected under 35 U.S.C. §112, First Paragraph, for containing subject matter that the Examiner contends was not described in the specification in such a way as to reasonably convey to one of skill in the art that the inventors had possession of the claimed invention at the time the application was filed. The Examiner bases this rejection on the use of the phrase "a fraction of their respective ED_{50} values."

It is Applicants' belief that given the knowledge and level of skill in the art, use of the term "a fraction of their respective ED_{50} values" within claim 72 would convey possession of the invention with reasonable clarity to one of skill in the art. However, solely in the interest of expediting prosecution, Applicants have amended claim 72 to remove the phrase cited above. Accordingly, this rejection has been obviated and Applicants request that it be withdrawn.

The Rejections of the Claims Under 35 U.S.C. §103(a) Should Be Withdrawn

Claims 67-71, 73-80, 84, and 88 are rejected under 35 U.S.C. §103(a) as being obvious in light of Kyle *et al.* (U.S. Patent No. 6,974,818), in view of Smith *et al.* (U.S. Patent No. 6,967,210). This rejection is traversed for the reasons provided below.

The claims of the present application are directed to pharmaceutical compositions comprising the $\alpha_2\delta$ subunit calcium channel modulators gabapentin or pregabalin in combination with the antimuscarinics oxybutynin, tolterodine, propiverine, or solifenacin monohydrochloride in therapeutically effective amounts sufficient to treat a symptom of a lower urinary tract disorders. These compositions are based upon Applicants' surprising discovery that the

combination of an $\alpha_2\delta$ subunit calcium channel modulator and an antimuscarinic produces a synergistic positive effect in the treatment of symptoms of lower urinary tract disorders.

The Examiner has suggested that Kyle *et al.* teach that oxybutynin may be combined with other active agents. Respectfully, this is a misreading of the Kyle *et al.* reference. The Kyle *et al.* reference is directed to "Thiadiazolylpiperazine Compounds" for use in treating a number of disorders, including pain, seizure, epilepsy, and urinary incontinence (see Column 1, lines 11-23). The thiadiazolylpiperazine compounds of Kyle *et al.* are described as inhibitors of vanilloid receptors and the metabotropic glutamate receptors mGluR1 and mGluR5 (see Column 33, line 55 to Column 35, line 53). These compounds are structurally and functionally unrelated to the antimuscarinic oxybutynin or the $\alpha_2\delta$ subunit calcium channel modulator gabapentin. Kyle *et al.* merely describe that the thiadiazolylpiperazine compounds of their invention may be used with other active agents, that oxybutynin is an agent known to be useful in the treatment of urinary incontinence, and that gabapentin is an agent known to be useful in the treatment of seizure and epilepsy (see, Column 1, lines 56-65; Column 6, lines 55-56; and Column 40, lines 22-40). The Kyle *et al.* patent does not teach or suggest a composition comprising gabapentin and oxybutynin, let alone specific dosages or amounts of active agents in such a combination that would be therapeutically effective in the treatment of symptoms of lower urinary tract disorders.

With respect to Smith *et al.*, the Examiner has suggested that this reference teaches a combination treatment comprising gabapentin for treatment of bladder irritation. However, this is also a misreading of the Smith *et al.* reference. The Smith *et al.* reference is directed to N-(pyridinyl)-1H-indol-amine compounds that may be useful for treating a number of disorders, including pain, demyelinating diseases, traumatic brain injury, and bladder irritation. The N-(pyridinyl)-1H-indol-amine compounds of Smith *et al.* are described as compounds that block both potassium and sodium channels (see Column 3, lines 44-47) and these compounds are structurally and functionally unrelated to the $\alpha_2\delta$ subunit calcium channel modulator gabapentin. Gabapentin is mentioned in the Smith *et al.* patent only for its known use in treating neuropathic pain. Specifically, gabapentin is used by Smith *et al.* as a positive control (see Example 9), in which the N-(pyridinyl)-1H-indol-amine compounds of the invention are tested for potential efficacy in the treatment of neuropathic pain. Accordingly, the Smith *et al.* patent does not teach

or suggest a combination treatment for bladder irritation, but instead describes compounds with a combination of blocking properties for both potassium and sodium channels. Furthermore, the Smith *et al.* patent does not teach or suggest that gabapentin may be used to treat bladder irritation, either alone or in combination with another active agent.

As the Examiner is aware, to establish a *prima facie* case of obviousness the prior art references must teach or suggest all the claim limitations and there must be some suggestion or motivation to modify or combine the reference teachings to arrive at the claimed invention. *In re Vaeck*, 947 F.2d 488 (Fed. Cir. 1991). For the reasons cited above, neither the Kyle *et al.* patent nor the Smith *et al.* patent, alone or in combination, teach or suggest the claimed compositions comprising the $\alpha_2\delta$ subunit calcium channel modulators gabapentin or pregabalin in combination with the antimuscarinics oxybutynin, tolterodine, propiverine, or solifenacin monohydrochloride. Accordingly, a *prima facie* case of obviousness has not been established and Applicants request that this rejection be withdrawn.

Claims 67-82, 84-86, and 88 are rejected under 35 U.S.C. §103(a) as being obvious in light of Kyle *et al.* in view of Christoph (U.S. Patent App. Pub. No. 20040242617). This rejection is traversed for the reasons provided below.

The limitations of the Kyle *et al.* reference in failing to teach or suggest every limitation of the present claims have been described above. The shortcomings of this reference (alone or in combination with Smith *et al.*) are not remedied by the additional citation of the Christoph reference. Christoph is directed to compositions comprising opioid compounds in combination with other agents, particularly antimuscarinics, and their use in treating urinary incontinence (see, *e.g.*, paragraph [0002]). Christoph teaches that oxybutynin, propiverine, and tolterodine are known treatments for urinary incontinence and may be combined with opioids for the same use (see, *e.g.*, paragraphs [0006] and [0082-0083]). However, Christoph fails to provide any teaching or suggestion of a composition comprising gabapentin and oxybutynin, let alone specific dosages or amounts of active agents in such a combination that would be therapeutically effective in the treatment of symptoms of lower urinary tract disorders. Accordingly, a *prima*

facie case of obviousness has not been established and Applicants request that this rejection be withdrawn.

Claims 83 and 87 are rejected under 35 U.S.C. §103(a) as being obvious in light of Kyle *et al.* in view of Takeuchi *et al.* (U.S. Patent No. 6,017,927). This rejection is traversed for the reasons provided below.

The limitations of the Kyle *et al.* reference in failing to teach or suggest every limitation of the present claims have been described above. The shortcomings of this reference (alone or in combination with Smith *et al.*) are not remedied by the additional citation of the Takeuchi *et al.* reference. The Takeuchi *et al.* reference is directed to compositions comprising quinuclidine derivatives including solifenacin hydrochloride and their use in treating urinary diseases (see, *e.g.*, Column 3, lines 60-66 and Column 4, lines 10-20). However, Takeuchi *et al.* fail to provide any teaching or suggestion of a composition comprising gabapentin and solifenacin, let alone specific dosages or amounts of active agents in such a combination that would be therapeutically effective in the treatment of symptoms of lower urinary tract disorders. Accordingly, a *prima facie* case of obviousness has not been established and Applicants request that this rejection be withdrawn.

The Provisional Obviousness-Type Double-Patenting Rejections Should Be Withdrawn

Claims 67-88 of the present application are provisionally rejected under the judicially created doctrine of obviousness-type double patenting over the claims of U.S. Patent Application Nos. 10/549,029 and 11/400,666. These rejections are respectfully traversed as applied to the currently pending claims.

Since none of the copending applications cited above have been allowed, Applicants submit that if the provisional nonstatutory obviousness-type double patenting rejections in view of these copending applications are the only rejections remaining in the present case, these rejections should be withdrawn and the present application allowed to issue as a patent without the need of a terminal disclaimer. See MPEP §804.I.B. Because Applicants believe that all

other rejections have been overcome in the present case, Applicants respectfully request that these nonstatutory obviousness-type double patenting rejections be withdrawn.

CONCLUSION

In view of the aforementioned claim amendments and remarks, Applicants submit that the rejection of the claims on the ground of nonstatutory double patenting and under 35 U.S.C. §§112 and 103(a) are overcome. Accordingly, Applicants submit that this application is now in condition for allowance. Early notice to this effect is solicited.

If in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject Application, the Examiner is invited to call the undersigned.

It is not believed that extensions of time or fees for net addition of claims are required, beyond those that may otherwise be provided for in documents accompanying this paper. However, in the event that additional extensions of time are necessary to allow consideration of this paper, such extensions are hereby petitioned under 37 CFR § 1.136(a), and any fee required therefore (including fees for net addition of claims) is hereby authorized to be charged to Deposit Account No. 16-0605.

Respectfully submitted,

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